Short-Term ADT and Dose-Escalated IMRT in Patients with Intermediate-Risk Prostate Cancer: Benefit or Caution?

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BACKGROUND / OBJECTIVES:

- In the era of dose-escalated prostate radiation therapy (RT), the use of androgen deprivation therapy (ADT) is undefined for intermediate-risk prostate cancer (IR).
- Randomized data demonstrates an improvement in biochemical control without an associated improvement in overall survival.
- There is also growing concern of the risk of ADT to be detrimental to quality of life and increase cardiac events
- This single-institution retrospective analysis aimed to evaluate outcomes of IR prostate cancer patients treated with RT with or without concurrent/adjuvant short-term ADT.

MATERIAL & METHODS

- Data was collected from 559 consecutive patients treated with dose-escalated IMRT with daily IGRT for newly diagnosed prostate cancer from December 2002 – March 2016.
- IMRT prescription was 78 Gy / 39 fractions or 70 Gy / 28 fractions.
- ADT was started near concurrently with RT, and consisted of a 30-day supply of bicalutamide, 50 mg daily. During that 30-day period, a GnRH agonist injection was initiated and continued for a total duration of 6 months
- Biochemical recurrence-free survival (BCRFS), distant metastasis-free survival (DMFS), prostate cancer-specific survival (PCSS), and overall survival (OS) were calculated using Kaplan-Meier methodology
- Cox proportional hazards modeling was used for univariate and multivariate analysis to assess the effect of several demographic and clinical factors on BCRFS and OS.

RESULTS

- Median follow-up of 93 months
- N=260 with IR disease, of which 69.6% (N=181) had UIR disease
- 78.8% (N=205) were treated with moderately hypofractionated RT to 70 Gy in 28 fractions
- 36.2% (N=94) received ADT, 89 UIR and 5 FIR, with median ADT duration of 6 months (range, 3-30; 90% received 6 months)
- When stratified by ADT use, baseline characteristics including mean age, baseline Charlson comorbidity index (CCI), and number of cardiovascular medications were equal between the two groups.

Table 1. Clinical characteristics of the IR Population

Characteristic	Intermediate-risk RT without ADT (N=166)	Intermediate-risk RT with ADT (N=94)	p value
Age (years)	66.9	67.3	0.49
CV Medications (N)	2.4	2.3	0.65
CCI	4.9	5.0	0.38
Pre-treatment PSA (ng/mL)	7.6	10.4	**< 0.001**
Clinical T Stage			**< 0.001**
cT1c – T2a	135 (81.3%)	58 (61.7%)	
cT2b – T2c	31 (18.7%)	36 (38.3%)	
Grade Group			**<0.001**
1 (GS 3+3)	11 (6.6%)	4 (4.3%)	
2 (GS 3+4)	129 (77.7%)	44 (46.8%)	
3 (GS 4+3)	26 (15.7%)	46 (48.9%)	
Risk Group			**< 0.001**
Favorable IR	74 (44.5%)	5 (5.3%)	
Unfavorable IR	92 (55.4%)	89 (94.7%)	
RT Fraction Size			**0.002**
2 Gy per fraction	45 (27.1%)	10 (10.6%)	
2.5 Gy per fraction	121 (72.9%)	84 (89.4%)	

CV, Cardiovascular; CCI, Charlson Comorbidity Index; PSA, Prostate Specific Antigen; GS, Gleason Score; IR, Intermediate-Risk; RT, Radiation Therapy; Gy, Grey; ADT, Androgen Deprivation Therapy

Outcomes:
- 7-year BCRFS
  ADT 94% vs no ADT 86% (p=0.067)
- 7-year DMFS
  ADT 99% vs no ADT 97% (NS)
- 7-year OS
  ADT 80% vs No ADT 91% (p=0.010)
  HR 2.02, 95% CI 1.17 – 3.50
- 7-year OS (< 70 years old)
  ADT 77% vs No ADT 93% (p=0.002)
  HR 3.03, 95% CI 1.46 – 6.27

Cause of Death Analysis:
- Cardiovascular disease (32.1%), other medical problems (28.3%), other cancer (15.1%), Unknown (24.5%)
- No difference in 7-year CV mortality-free survival between ADT vs No ADT groups (95% vs. 96%)

Figure 1. (a) BCRFS and (b) OS for IR patients treated with and without ADT

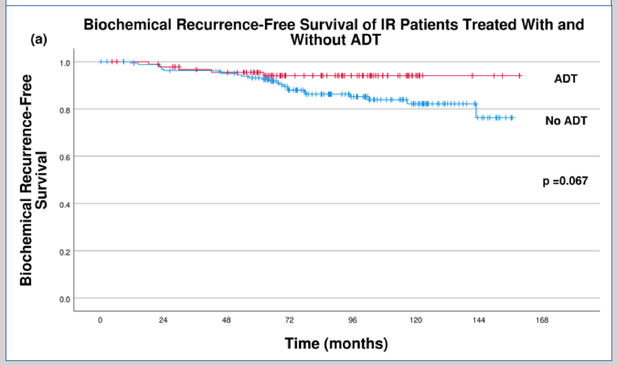
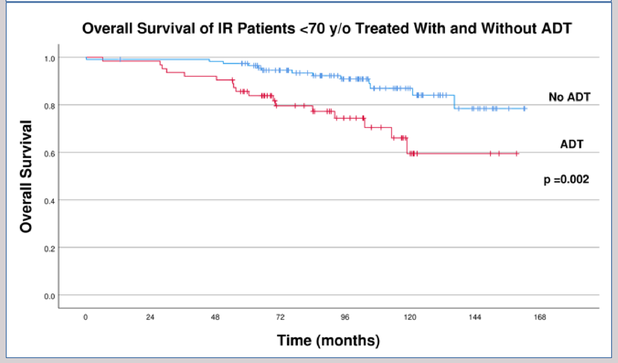


Figure 2. OS for IR patients <70 treated with and without ADT



SUMMARY / CONCLUSION

- The evidence that endorses short-term ADT in IR prostate cancer is not based on modern/volume-based radiation techniques and delivery.
- Our experience represents **one of the largest retrospective studies available with consistent utilization of IMRT and daily IGRT** with or without short-term concurrent/adjuvant ADT.
- Although our analysis did not show statistical significance, the trend supports the well-known benefit of ADT in regards to biochemical control.
- Locoregional recurrence (N=6, 2.3%), distant metastasis (N=8, 3.1%) and death from prostate cancer (N=0) were low within our IR cohort.
- The most intriguing finding of this study was the **large decrement in overall survival observed for patients who received short-term ADT**, which equated to an **absolute difference of 11% at 7 years**. This was limited to patients < 70 years old.
- There was no observed difference in cardiovascular mortality between groups.

- Strengths:
- Consistent use of dose-escalated IMRT and daily IGRT.
- long follow-up (median 7.75 years).
- Few patients lost to follow-up, with 95.4% of patients reaching at least 3 years of follow-up.

- Limitations:
- Unknown/unwitnessed cause of death was almost 25%.
- Retrospective Study

ACKNOWLEDGEMENTS

We would like to thank our patients, Oregon Health & Sciences University, the Portland VA Medical Center, and all providers involved in the care of our patients.

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